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Higher incidence and persistence of high-risk human papillomavirus infection in female sex workers compared with women attending family planning

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SUMMARY

Background: There are no data on the incidence and persistence of high-risk human papillomavirus (HR-HPV) infections in female sex workers (FSWs). We aimed to describe and compare the rates of incidence and persistence of HR-HPV infections in FSWs and women from the general population (WGP) who attended healthcare facilities between May 2003 and December 2006 in Alicante, Spain.

Methods: Women with an established HR-HPV infection at study entry were evaluated for the analysis of HR-HPV persistence, and those testing negative for HR-HPV infection at entry were evaluated for the analysis of incidence. HR-HPV infection was determined by the Digene HC2 HR HPV DNA Test.

Results: A total of 736 women – 592 WGP and 144 FSWs – were followed for a median of 16.8 months. Global incidence and persistence rates were 3.98 per 100 woman-years (95% confidence interval (CI) 2.91–5.45) and 26.81 per 100 woman-years (95% CI 20.08–35.79), respectively. In the multivariate analysis, only commercial sex work was associated with a statistically significant higher incidence (relative risk (RR) 4.72, 95% CI 2.45–9.09) and persistence (RR 1.93, 95% CI 1.08–3.46) of HR-HPV infection.

Conclusions: Our data show that FSWs have both a higher incidence and a higher persistence of HR-HPV than WGP and should be prioritized in HPV-related cancer screening programs.

1. Introduction

Human papillomavirus (HPV) infection is the most frequent sexually transmitted infection (STI) worldwide. High-risk HPV (HR-HPV) is the main cause of cervical cancer.[1] Population groups with higher prevalences of infection, like women who are incarcerated or female sex workers (FSWs), usually have sexual risk behaviours.[2–4] In women in the general population (WGP), over half clear the virus spontaneously within a year of contracting the infection. A higher risk of developing cervical cancer exists only in the small proportion of cases with persistent infection, and in the presence of other co-factors like oral contraceptive use, smoking, or high parity.[5] Trottier et al. recently reported that infection with multiple HPV types is associated with longer persistence of HPV infection, but that this is not the case for either age or number of sexual partners.[6] The prevalence of infection includes all those established cases that do not clear spontaneously, as well as all incident cases. Accordingly, HPV prevalence is influenced by risk factors associated with both the incidence and the persistence of infection. In comparison to prevalence studies, fewer studies have been carried out on the incidence of HR-HVP infection in WGP and none in the population in Spain. To our knowledge, there have been no publications on the incidence and persistence of global HR-HPV infection in FSWs.

The aim of this study was to describe and compare the incidence and persistence of HR-HPV infections in FSWs and in WGP who attended a healthcare facility between May 2003 and December 2006 in the city of Alicante, Spain.

2. Methods

2.1. Study population

We conducted a prospective study with a cohort of WGP and FSWs recruited at two sites in the city of Alicante, Spain. WGP were recruited at a family planning clinic and FSWs at the Center for AIDS Information and Prevention (CIPS). Both health facilities are free of charge to all women, including immigrant women irrespective of their legal and administrative status. Women were invited to participate in the study between May 2003 and

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December 2004 and were followed annually or more frequently if clinically indicated, up to December 2006. Characteristics of each of the recruitment sites and baseline HR-HPV prevalence for WGP and FSWs have been described previously,[3,7] and are also presented in Table 1. For the purpose of these analyses, only women who had at least two HR-HPV test results separated by a minimum of approximately 6 months were included. Some women made more visits to the clinic, but we only analyzed the incidence and persistence between the first two visits. Figure 1 shows the number of women participating in each of the analyses; women with an established HR-HPV infection at study entry were evaluated for the analysis of HR-HPV persistence, and those testing negative for HR-HPV infection at study entry were evaluated for the analysis of HR-HPV incidence. We considered incident infections as those occurring in women whose sample tested HR-HPV-positive following an initial sample that tested negative. We considered persistent infections as those occurring in women whose sample tested HR-HPV-positive following an initial sample that tested positive. Additional analyses were done to look for statistically significant differences in the socio-demographic characteristics, sexual behaviors, and HPV prevalence between women who failed to return and those who were followed up, stratified by center.

The two dependent variables were incident and persistent HR-HPV infections determined by the Digene Hybrid Capture 2, High-Risk HPV DNA Test (HC2 HR HPV DNA Test; Qiagen, Germany). Detection of HR-HPV DNA in a woman who had a negative HR-HPV DNA test at study entry was considered to be an incident infection. Persistent infections were those cases that tested positive both at study entry and during follow-up. The main independent variable, being a FSW as compared to a WGP, was ascertained from the recruitment site; FSWs were recruited at a FSW opt-in specialist clinic with a long-standing tradition of treating FSWs, and WGP from a family planning center where they were not specifically asked whether they had ever exchanged sex for money. Most of the women from the general population in Alicante go to family planning centers for gynecological and routine exams. We also collected information on age at entry (≤25, 26–35, ≥36 years, and unknown), age at first sexual intercourse (≤18, ≥19 years, and unknown), area of origin (Spain, Latin America, Europe, and Africa/Asia; these last two were recoded as 'other' because of the small number of people from these regions), educational level (none,

Table 1
Characteristics of study subjects at baseline and follow-up

	WGP			FSWs			Total		
	Baseline *n* (%)	Follow-up *n* (%)	*p*-Value	Baseline *n* (%)	Follow-up *n* (%)	*p*-Value	Baseline *n* (%)	Follow-up *n* (%)	*p*-Value
	(*n* = 1011)	(*n* = 592)		(*n* = 549)	(*n* = 144)		(*n* = 1560)	(*n* = 736)	
Age			0.0222			0.4799			0.0039
≤25 years	274 (27.1)	123 (20.8)		185 (33.7)	47 (32.6)		459 (29.4)	170 (23.1)	
26–35 years	367 (36.3)	217 (36.7)		228 (41.5)	63 (43.8)		595 (38.1)	280 (38.0)	
≥36 years	366 (36.2)	250 (42.2)		134 (24.4)	32 (22.2)		500 (32.1)	282 (38.3)	
Unknown	4 (0.4)	2 (0.3)		2 (0.4)	2 (1.4)		6 (0.4)	4 (0.5)	
Area of origin			0.8964			0.0134			0.0000
Spain	841 (83.2)	501 (84.6)		87 (15.8)	21 (14.6)		928 (59.5)	522 (70.9)	
Latin America	122 (12.1)	66 (11.1)		303 (55.2)	76 (52.8)		425 (27.2)	142 (19.3)	
Europe	32 (3.2)	17 (2.9)		91 (16.6)	15 (10.4)		123 (7.9)	32 (4.3)	
Africa/Asia	16 (1.6)	8 (1.4)		68 (12.4)	32 (22.2)		84 (5.4)	40 (5.4)	
Educational level			0.0572			0.0000			0.0000
None	62 (6.1)	33 (5.6)		38 (6.9)	14 (9.7)		100 (6.4)	47 (6.4)	
Primary education	344 (34.0)	195 (32.9)		419 (76.3)	44 (30.6)		763 (48.9)	239 (32.5)	
High school	604 (59.7)	358 (60.5)		50 (9.1)	73 (50.7)		654 (41.9)	431 (58.6)	
Unknown	1 (0.1)	6 (1.0)		42 (7.7)	13 (9.0)		43 (2.8)	19 (2.6)	
Number of lifetime sex partners			0.9284			0.4314			0.0001
≤5	903 (89.3)	528 (89.2)		235 (42.8)	56 (38.9)		1138 (72.9)	584 (79.3)	
>5	107 (10.6)	63 (10.6)		19 (3.5)	3 (2.1)		126 (8.1)	66 (9.0)	
Unknown	1 (0.1)	1 (0.2)		295 (53.7)	85 (59.0)		296 (19.0)	86 (11.7)	
Marital status			0.2208			0.8443			0.0001
Single	370 (36.6)	196 (33.1)		300 (54.6)	75 (52.1)		670 (42.9)	271 (36.8)	
Married	464 (45.9)	301 (50.8)		54 (9.8)	17 (11.8)		518 (33.2)	318 (43.2)	
Lives with partner	101 (10.0)	49 (8.3)		63 (11.5)	17 (11.8)		164 (10.5)	66 (9.0)	
Separated/ divorced/widow	76 (7.5)	46 (7.8)		129 (23.5)	35 (24.3)		205 (13.1)	81 (11.0)	
Unknown	0	0		3 (0.5)	0		3 (0.2)	0	
Age at first sexual intercourse, median (range)	18 (17–20)	18 (17–20)	-	17 (15–18)	16 (14–17)	-	18 (16–19)	18 (16–19)	-
Unknown	1	0		62	15		63	15	
Smoking in last year			0.7484			0.0074			0.0002
No	516 (51.0)	312 (52.7)		268 (48.8)	69 (47.9)		784 (50.3)	381 (51.8)	
Yes	494 (48.9)	279 (47.1)		242 (44.1)	61 (42.4)		736 (47.2)	340 (46.2)	
Unknown	1 (0.1)	1 (0.2)		39 (7.1)	14 (9.7)		40 (2.6)	15 (2.0)	
HIV result			0.0894			0.1095			0.1870
Negative	448 (44.3)	271 (45.8)		293 (53.4)	69 (47.9)		741 (47.5)	340 (46.2)	
Positive	3 (0.3)	2 (0.3)		16 (2.9)	1 (0.7)		19 (1.2)	3 (0.4)	
Unknown	560 (55.4)	319 (53.9)		240 (43.7)	74 (51.4)		800 (51.3)	393 (53.4)	
Duration of follow-up (months), median (range)	17.7 (14–26)			14.2 (11.5–16.7)			16.8 (13.4–23.2)		

WGP, women from the general population; FSWs, female sex workers.

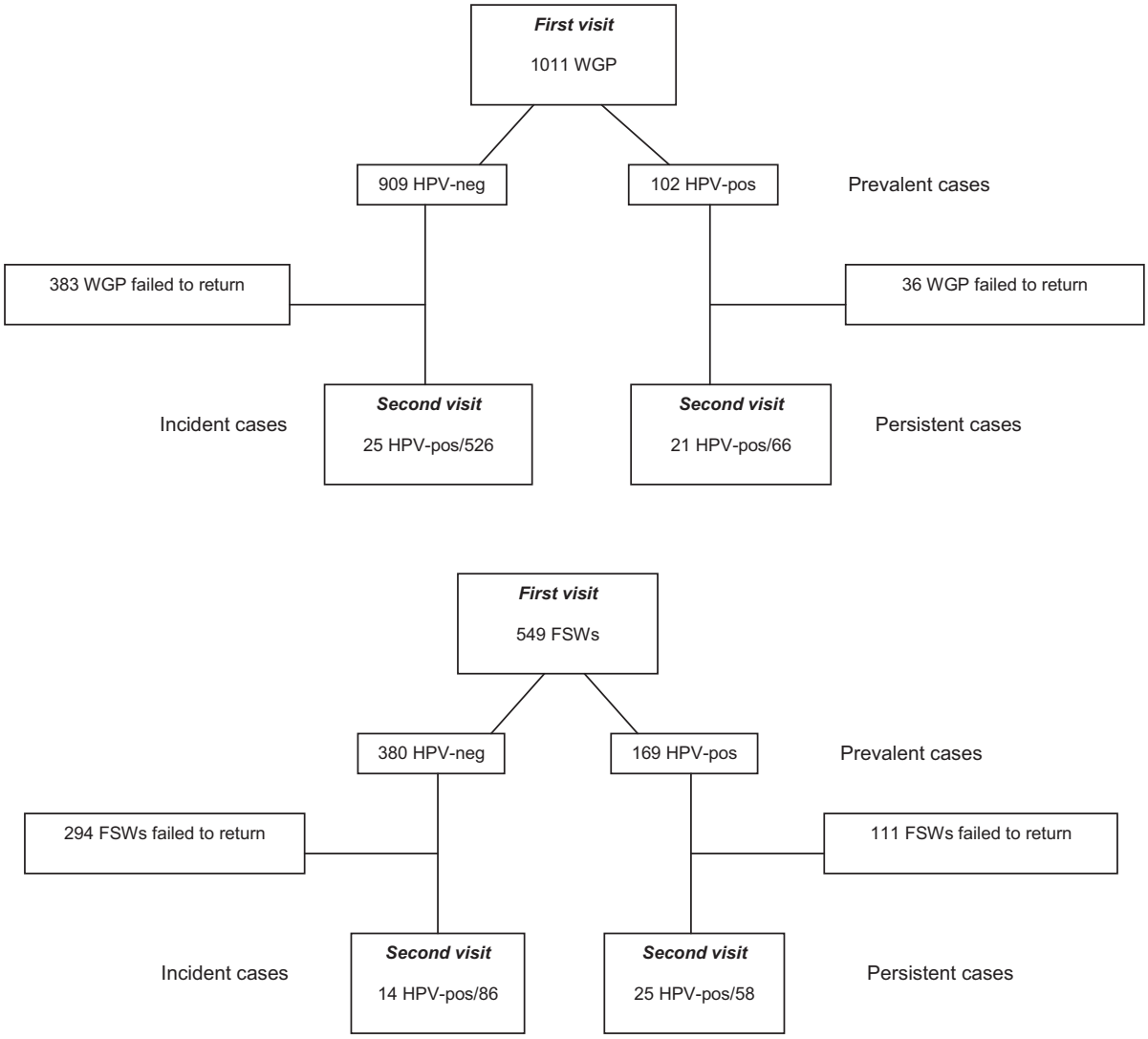

Figure 1. Flow chart of participants (WGP: women from the general population; FSWs: female sex workers).

primary, high school, and unknown), civil status (single, married, lives with partner, separated/divorced/widowed, and unknown), number of life-time private sexual partners (≤ 5, > 5, and unknown), smoking (no, yes, and unknown), and HIV status (negative, positive, and unknown). HIV status was self-reported for WGP recruited at the family planning center, and an HIV test was done for FSWs at the Center for AIDS Information and Prevention.

All the women who agreed to participate in the study gave oral consent to an informed consent statement which was approved by the Ethics Committee of the Universidad Miguel Hernández de Elche (Alicante, Spain). The present study was carried out before the new law approved in Spain in 2007 in relation to biomedical research, hence oral consent was allowed.

2.2. High-risk HPV detection

HR-HPV infection was determined by the HC2 HR HPV DNA Test, which identifies types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68. All cervical samples were taken using a cervical brush and placed in Digene Specimen Transport Medium and stored at $-20\ ^{\circ}C$ until required for testing. The HC2 HR HPV DNA Test was performed following the manufacturer's instructions. In brief, the exfoliated cells are first treated with alkaline denaturation reagent, and the processed samples are hybridized under high-stringency conditions. Positive specimens are detected by binding the hybridization complexes onto the surface of a microplate well coated with monoclonal antibodies specific to RNA–DNA hybrids. Immobilized hybrids are detected by the addition of an alkaline phosphatase-conjugated antibody to RNA–DNA hybrids, followed by the addition of a chemiluminescent substrate. Samples were analyzed at the National Center of Microbiology in Madrid, Spain.

2.3. Statistical methods

Descriptive analyses of demographic characteristics and clinical parameters were carried out using frequency distributions or median and interquartile ranges (IQR) as appropriate. Baseline characteristics of women who returned to the recruiting sites for a second visit were compared to those who were lost to follow-up. Differences were tested by Mann–Whitney *U*-test and Chi-square test as appropriate. We calculated the HR-HPV incidence and persistence rates as the number of events divided by the total number of woman-years of follow-up. Analyses using woman-months were also performed. The date of administrative censoring was December 2006. We modeled relative rates by multivariate Poisson regression analyses using a forward approach with all the

variables of the study. Analyses were carried out in STATA 10 (StataCorp LP, College Station, TX, USA).

3. Results

The cohort included 736 women: 592 WGP who were followed for an average of 17.7 months (IQR 14–26) and 144 FSWs who were followed for a median of 14.2 months (IQR 11.5–16.7). Socio-demographic and sexual behavior characteristics of the women are shown in Table 1. The median age at study entry was 34 years (IQR 27–41) in WGP and 29 years (IQR 24–35) in FSWs. Overall, 501 (84.6%) WGP were Spanish and 76 (52.8%) FSWs were Latin American. A total of 528 (89.2%) WGP reported fewer than five lifetime sexual partners and 85 (59%) FSWs did not report their number of lifetime sexual partners. Median age at first sexual intercourse was 18 years (IQR 17–20) in WGP and 16 years (IQR 14–17) in FSWs. Self-reported prevalence of HIV infection in the 273 WGP for whom this information was available was 0.3%, versus 0.7% in 70 FSWs. The median time between HR-HPV test results was 16.8 months (IQR 13.4–23.2) for all women.

Approximately 76.5% of WGP had used condoms sometime in the past, and 32.7% had used them in the 6 months before the first visit. In the case of FSWs, 99.2% had used condoms in the past and in the last 6 months. Of the FSWs who had used condoms both in the last 6 months and previously, 94.4% used them always or almost always in vaginal coitus with clients, and 10.7% did so with their regular partners.

We analyzed differences between women who attended only one visit and those who were followed on more than one occasion. Among FSWs, 110 made only one visit and their HR-HPV prevalence was 27.2%, and 59 had made more than one visit and their HR-HPV prevalence was 40.7%; this difference was statistically significant ($p = 0.003$). The same pattern was observed in WGP: 36 made only one visit and their HR-HPV prevalence was 8.6%, and 66 were followed up and their HR-HPV prevalence was 11.1%; however, the difference in this latter case was not statistically significant ($p = 0.198$). The proportion of WGP over 36 years of age was higher among those returning for a second visit (42.2% vs. 27.6%, $p < 0.001$) than those who came only once. The percentage of married WGP was higher in those who were followed at a second visit than in those who came only once (50.8% vs. 38.8%, $p = 0.001$).

3.1. Incidence of HR-HPV infection

The overall incidence rate was 3.98 per 100 woman-years (95% CI 2.91–5.45) or 0.33 per 100 woman-months (95% CI 0.24–0.45). This rate was lower in WGP (2.85 per 100 woman-years (95% CI 1.92–4.22) or 0.23 per 100 woman-months (95% CI 0.16–0.35)) than in FSWs (13.5 per 100 woman-years (95% CI 7.99–22.79) or 1.12 per 100 woman-months (95% CI 0.66–1.90)). Table 2 shows the rates of incidence of HR-HPV infection per 100 woman-years for WGP and FSWs.

The crude relative risks (RR) of HR-HPV incidence are presented in Table 3. The risk of infection was almost five times higher in FSWs than in WGP (RR 4.72, 95% CI 2.45–9.09). The risk of infection was lower in Spanish women (RR 0.34, 95% CI 0.16–0.68) than in Latin Americans, and was lower in married women (RR 0.43, 95% CI

Table 2
Incidence rates of HR-HPV infection

	Person-years		Number of incident cases		Rate/100 woman-years (95% CI)	
	WGP	FSWs	WGP	FSWs	WGP	FSWs
Age						
≤25 years	171.64	26.27	6	4	3.49 (1.57–7.78)	15.22 (5.71–40.56)
26–35 years	336.23	46.58	12	6	3.56 (2.02–6.28)	12.87 (5.78–28.66)
≥36 years	365.22	28.58	7	3	1.91 (0.91–4.02)	10.49 (3.38–32.53)
Unknown	2.20	2.26	0	1	-	44.23 (6.23–314.01)
Area of origin						
Spain	750.22	15.93	22	0	2.93 (1.93–4.45)	-
Latin America	85.16	57.18	3	9	3.52 (1.13–10.92)	15.73 (8.18–30.24)
Other	39.91	30.58	0	5	-	16.34 (6.80–39.27)
Educational level						
None	56.34	7.20	0	2	-	27.77 (6.94–111.04)
Primary education	293.68	37.72	7	3	2.38 (1.13–4.99)	7.95 (2.56–24.650)
High school	514.32	47.94	18	8	3.49 (2.20–5.55)	16.68 (8.34–33.36)
Unknown	10.94	10.84	0	1	-	9.22 (1.29–65.47)
Number of lifetime sex partners						
≤5	794.57	38.02	23	3	2.89 (1.92–4.35)	7.89 (2.54–24.46)
>5	78.65	3.37	2	2	2.54 (0.63–10.16)	59.20 (14.80–236.31)
Unknown	2.06	62.30	0	9	-	14.44 (7.51–27.76)
Marital status						
Single	278.60	54.34	9	8	3.23 (1.68–6.20)	14.72 (7.36–29.43)
Married	479.07	11.97	10	1	2.08 (1.12–3.87)	8.35 (1.17–59.29)
Lives with partner	58.25	12.86	3	1	5.14 (1.66–15.96)	7.77 (1.09–55.18)
Separated/divorced/widowed	59.37	24.52	3	4	5.05 (1.62–15.66)	16.30 (6.12–43.45)
Smoking in last year						
No	463.87	53.10	13	9	2.80 (1.62–4.82)	16.94 (8.81–32.57)
Yes	409.60	42.23	12	3	2.92 (1.66–5.15)	7.10 (2.29–22.02)
Unknown	1.81	-	0	-	-	-
HIV result						
Negative	394.42	46.50	8	5	2.02 (1.01–4.05)	10.75 (4.47–25.83)
Positive	3.81	-	0	-	-	-
Unknown	477.06	57.19	17	9	3.56 (2.21–5.73)	15.73 (8.18–30.24)
Age at first sexual intercourse						
≤18 years	524.36	78.77	18	11	3.43 (2.16–5.44)	13.96 (7.73–25.21)
≥19 years	350.93	17.03	7	2	1.99 (0.95–4.18)	11.73 (2.93–46.93)
Unknown	-	7.89	-	1	-	12.67 (1.78–89.96)

HR-HPV, high-risk human papillomavirus; CI, confidence interval; WGP, women from the general population; FSWs, female sex workers.

Table 3
Univariate analyses of the relative risk of HR-HPV incidence

	RR (95% CI)
Age	
≤25 years	1
26–35 years	0.93 (0.42–2.01)
≥36 years	0.50 (0.20–1.20)
Unknown	4.43 (0.56–34.64)
Area of origin	[a]
Spain	0.34 (0.16–0.68)
Latin America	1
Others	0.84 (0.29–2.38)
Educational level	
None	1
Primary education	0.95 (0.21–4.37)
High School	1.46 (0.34–6.19)
Unknown	1.45 (0.13–16.08)
Number of lifetime sex partners	
≤5	1
>5	1.56 (0.54–4.47)
Unknown	4.47 (2.09–9.55)
Marital status	[a]
Single	1
Married	0.43 (0.20–0.93)
Lives with partner	1.10 (0.37–3.27)
Separated/divorced/widowed	1.63 (0.67–3.94)
Smoking in last year	
No	1
Yes	0.78 (0.40–1.50)
Unknown	-
HIV result	
Negative	1
Positive	-
Unknown	1.65 (0.84–3.21)
Age at first sexual intercourse	
≤18 years	1
≥19 years	0.50 (0.24–1.07)
Unknown	2.63 (0.35–19.34)
Recruitment	[b]
WGP	1
FSWs	4.72 (2.45–9.09)

HR-HPV, high-risk human papillomavirus; RR, relative risk; CI, confidence interval; WGP, women from the general population; FSWs, female sex workers.
[a] p-Value of homogeneity < 0.05.
[b] p-Value of homogeneity < 0.001.

0.20–0.93) than in those who were single. The only variable that remained associated with the incidence of HR-HPV infection in the multivariate analysis was engaging in prostitution (RR 4.72, 95% CI 2.45–9.09); the relative risk of infection in FSWs was the same in the multivariate analysis as in the univariate analysis.

3.2. Persistence of HR-HPV infection

The overall rate of persistence was 26.81 per 100 woman-years (95% CI 20.08–35.79) or 2.23 per 100 woman-months (95% CI 1.67–2.98). Similar to the results for incidence rates, persistence was lower in WGP (19.8 per 100 woman-years (95% CI 12.88–30.31) or 1.64 per 100 woman-months (95% CI 1.07–2.52)) than in FSWs (38.28 per 100 woman-years (95% CI 25.86–56.65) or 3.19 per 100 woman-months (95% CI 2.15–4.72)).

Table 4 shows the rates of persistence of HPV infection per 100 woman-years for WGP and FSWs.

The crude relative risks of HR-HPV persistence are presented in Table 5. The risk of persistence was lower in Spanish women (RR 0.71, 95% CI 0.37–1.36) than in Latin Americans, and was lower in married women (RR 0.77, 95% CI 0.34–1.72) than in those who were single, although these differences were not statistically significant. Women who engaged in prostitution had nearly double the risk of persistent HR-HPV infection (RR 1.93, 95% CI 1.08–3.46), a risk that was maintained in the multivariate analysis with the same relative risk.

4. Discussion

The rates of HR-HPV incidence and persistence were significantly higher in FSWs than in WGP, differences that were more marked in the case of incidence than persistence of HR-HPV infection. The incidence of HR-HPV in FSWs was 13.51 per 100 woman-years and in WGP was 2.85 per 100 woman-years. The persistence of HR-HPV in FSWs was 38.28 per 100 woman-years and in WGP was 19.76 per 100 woman-years. The only risk factor identified in this study for the incidence and persistence of HR-HPV infection was engaging in prostitution.

Prostitution was associated with a five-fold greater risk of acquiring HR-HPV than in WGP. In fact, the only risk factor associated with the incidence of HR-HPV found in this work was being a FSW. Although a higher incidence in Latin American and single women was found in the univariate analysis, these differences disappeared in the multivariate analysis since they reflect characteristics of FSWs. The only risk factor associated with the persistence of HR-HPV infection was engaging in prostitution. The risk of persistent infection in FSWs was double that in WGP. These data suggest that, although the incidence of infection seems to be more closely associated with sexual risk behaviors, these appear to be less important in explaining the persistence of infection. However this finding should be interpreted with caution since we are not assessing the persistence of incident infections but of established ones.

As far as we know, these are the first data published on the incidence and persistence of HR-HPV in both FSWs and WGP in Spain, so they cannot be compared with findings of previous publications in our country. The high incidence in FSWs compared with WGP could be expected, but there has not yet been any paper published on this. The incidence of HR-HPV infections in WGP in our study from Alicante is, nevertheless, lower than that reported by authors from the USA, Canada, and other European countries. The cumulative incidence of HR-HPV infection in young women in the USA was around 40% at 3 years[8,9] and 32.3% at 2 years.[10,11] In a gynecology center in Arizona, the incidence rate for any type of HPV in women between age 18 and 35 years was 2.9% per month, with higher proportions for oncogenic types.[12] In Canada, the HR-HPV incidence rate in university women was 14 per 1000 woman-months.[13] In Brazil, the incidence of infection was 6.8 per 1000 woman-months (95% CI 5.4–8.4) in women of low socioeconomic status aged between 18 and 60 years.[14] In the former Soviet Union, the overall rate of incident HR-HPV infections was 1.0 per 100 woman-months at risk.[15] In Denmark, the overall 2-year incidence of HR-HPV infection in initially HPV-negative women was 12.8% (95% CI 12.0–13.6).[16] Although no HPV incidence data have previously been published in Spain, the prevalence of HPV infection in Spain is one of the lowest in the world; de Sanjosé et al., in the only population-based work to-date in Spain, reported a prevalence of HPV infection in women in the general population of 3%.[17] Spain also has one of the lowest incidence rates of cervical cancer, around 7%.[1]

With regard to persistence of HR-HPV infection, Franco et al. observed that 61% (95% CI 54–69) of a cohort of women in Brazil remained infected at 6 months, and only 35% (95% CI 27–42) after 12 months.[14] Sellors et al. reported a persistence of 48% (26/54) after a median of 14 months in women in Canada.[18] In a gynecology center in Arizona, the percentage of persistent infection from any type of HPV was 50.3% in women who had had more than two visits.[12] The persistence of HR-HPV infection in WGP in our study is lower than that described in previously published studies.[12,14,18]

Our findings on the incidence or persistence of HR-HPV in FSWs cannot be compared with other studies as there are no previous publications in this group of women; the sexual and reproductive

Table 4
Persistence of HR-HPV infection

	Person-years		Number of persistent cases		Rate/100 woman-years (95% CI)	
	WGP	FSWs	WGP	FSWs	WGP	FSWs
Age						
≤25 years	32.91	30.98	8	14	24.30 (12.15–48.59)	45.18 (26.76–76.30)
26–35 years	28.81	25.91	4	8	13.88 (5.21–36.98)	30.87 (15.43–61.73)
≥36 years	44.52	8.41	9	3	20.21 (10.51–38.84)	35.65 (11.49–110.54)
Unknown	-	-	-	-	-	-
Area of origin						
Spain	75.89	10.85	15	3	19.76 (11.91–32.78)	27.63 (8.91–85.67)
Latin America	28.18	33.59	4	14	14.19 (5.32–37.80)	41.66 (24.67–70.35)
Other	2.17	20.84	2	8	92.12 (23.04–368.37)	38.36 (19.18–76.72)
Educational level						
None	1.84	9.26	0	2	-	21.58 (5.39–86.30)
Primary education	32.04	13.11	7	5	21.84 (10.41–45.82)	38.13 (15.87–91.62)
High School	72.36	36.04	14	17	19.34 (11.45–32.66)	47.16 (29.32–75.87)
Unknown	-	6.88	-	1	-	14.51 (2.04–103.05)
Number of lifetime sex partners						
≤5	84.88	26.21	13	10	15.31 (8.89–26.37)	38.14 (20.52–70.88)
>5	21.37	0.99	8	0	37.42 (18.71–74.83)	-
Unknown	-	38.09	-	15	-	39.37 (23.73–65.31)
Marital status						
Single	43.09	34.11	9	15	20.88 (10.86–40.13)	43.97 (26.50–72.93)
Married	26.21	7.08	4	4	15.25 (5.72–40.65)	56.42 (21.17–150.34)
Lives with partner	19.73	7.02	5	2	25.34 (10.54–60.88)	28.48 (7.12–113.89)
Separated/divorced/widowed	17.21	17.08	3	4	17.42 (5.62–54.04)	23.41 (8.78–62.38)
Smoking in last year						
No	42.66	25.63	5	12	11.71 (4.87–28.15)	46.81 (26.58–82.42)
Yes	63.59	31.54	16	12	25.16 (15.41–41.07)	38.03 (21.60–66.97)
Unknown	-	-	-	-	-	-
HIV result						
Negative	59.49	33.27	12	13	20.16 (11.45–35.51)	39.06 (22.68–67.28)
Positive	-	1.26	-	0	-	-
Unknown	46.75	30.76	9	12	19.24 (10.01–36.99)	38.99 (22.14–68.67)
Age at first sexual intercourse						
≤18 years	77.26	54.39	14	20	18.11 (10.73–30.59)	36.76 (23.72–56.99)
≥19 years	28.98	2.42	7	1	24.14 (11.51–50.65)	41.27 (5.81–292.99)
Unknown	-	8.49	-	4	-	47.10 (17.67–125.50)

HR-HPV, high-risk human papillomavirus; CI, confidence interval; WGP, women from the general population; FSWs, female sex workers.

Table 5
Univariate analyses of the relative risk of HR-HPV persistence

	RR (95% CI)
Age	
≤25 years	1
26–35 years	0.63 (0.31–1.28)
≥36 years	0.65 (0.32–1.33)
Unknown	-
Area of origin	
Spain	0.71 (0.37–1.36)
Latin America	1
Other	1.49 (0.68–3.23)
Educational level	
None	1
Primary education	1.47 (0.33–6.59)
High School	1.58 (0.38–6.64)
Unknown	0.80 (0.07–8.89)
Number of lifetime sex partners	
≤5	1
>5	1.72 (0.77–3.86)
Unknown	1.90 (0.99–3.64)
Marital status	
Single	1
Married	0.77 (0.34–1.72)
Lives with partner	0.84 (0.36–1.95)
Separated/divorced/widowed	0.65 (0.28–1.52)
Smoking in last year	
No	1
Yes	1.18 (0.64–2.16)
Unknown	-
HIV result	
Negative	1
Positive	-
Unknown	1.00 (0.56–1.79)
Age at first sexual intercourse	
≤18 years	1
≥19 years	0.98 (0.45–2.13)
Unknown	1.82 (0.64–5.14)
Recruitment	[a]
WGP	1
FSWs	1.93 (1.08–3.46)

HR-HPV, high-risk human papillomavirus; RR, relative risk; CI, confidence interval; WGP, women from the general population; FSWs, female sex workers.
[a] p-Value of homogeneity < 0.05.

health of FSWs has not been sufficiently studied. Analysis of condom use in FSWs showed differences between their use with clients and with regular partners. Condom use with clients was nearly 100%, whereas the percentage using condoms with regular partners was lower. Similar results have been reported by del Amo et al. in the same cohort of FSWs in Alicante[3] and by Belza et al. in a study in FSWs in Madrid.[19] Although condoms do not offer 100% protection against HR-HPV, Winer et al. have described a reduced risk associated with systematic use.[20] Thus, in addition to insisting on the need for consistent condom use with clients, the role of private partners as sources of HR-HPV infection, as well as other sexually transmitted infections, cannot be neglected.

The non-significance of some of the risk factors in our work may well have been due to the lack of statistical power, the main limitation in this type of study. Losses to follow-up are particularly high in FSWs, a group that is difficult to retain in a follow-up study,

given their working, social, and legal characteristics. Persistent infections may include the clearance of one HPV genotype together with incident infection by another type. Unfortunately we did not calculate type-specific incidence or persistence in this study. Among FSWs, those with an established HR-HPV infection were more likely to return for a second visit. Given the high losses to follow-up in FSWs, the incidence estimates have to be interpreted with caution, but highlight the higher incidence of HR-HPV in this group; it is expected that HPV incidence may be even higher among FSWs not accessing healthcare services.

In summary, these are the first data published on the incidence and persistence of HR-HPV in Spain and, to our knowledge, the first data published on these outcomes in FSWs. Our data show that FSWs have both a higher incidence and a higher persistence of HR-HPV than WGP, thus they should be prioritized in HPV-related cancer screening programs. In this respect, supporting clinics that treat the high-risk population are important in the fight against cervical cancer in vulnerable populations.

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Ethical approval: The present study was carried out before the new law approved in Spain in 2007 in relation to biomedical research, hence the oral consent was allowed. All the women who agreed to participate in the study gave oral consent to an informed consent statement which was approved by the Ethics Committee of the Universidad Miguel Hernández de Elche (Alicante, Spain).

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